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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LONG, SCOTT	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,038	SLACK ET AL.	
	Examiner	Art Unit	
	SCOTT LONG	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6-13 and 18-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6-13 and 18-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner acknowledges receipt of Applicant's Remarks, filed on 12 August 2008.

Claim Status

No claims are amended in the claim set submitted 8/12/2008. Claims 3-5 and 14-17 are cancelled. Claims 1-2, 6-13, and 18-34 are under current examination.

Priority

This application claims benefit as a 371 of PCT/CH03/00830 (filed 12/17/2003) which claims benefit of 60/434,790 (filed 12/18/2002). The instant application has been granted the benefit date, 18 December 2002, from the application 60/434,790.

Response to Arguments - Claim Rejections 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 6-13, and 18-34 remain rejected under 35 U.S.C. 103(a) as being obvious over Margolskee (US-5,817,759, issued 6 October 1998) in view of Yao et al. (US-7,041,457, issued 9 May 2006) and further in view of Ruiz-Avila et al. (PNAS. July 17 2001. vol.98; No.15: 8868-8873) for the reasons of record and the comments below.

Applicant's arguments (Remarks, pages 9-18) have been fully considered but are not persuasive.

Therefore, the examiner hereby maintains the rejection of Claims 1-2 and 10-13 under 35 U.S.C. 103(a) as being obvious over Margolskee (US-5,817,759, issued 6 October 1998) in view of Yao et al. (US-7,041,457, issued 9 May 2006) and further in view of Ruiz-Avila et al. (PNAS. July 17 2001. vol.98; No.15: 8868-8873).

The applicant has made several arguments in traversal of the instant rejection.

The arguments on page 9 seem to be suggesting that (1) the combination of the cited art does not suggest a $G_{\alpha q\text{-Gustducin}}$ chimeric G-protein comprising a substituted 44 amino acid carboxy terminus and (2) the "low 58% homology" between gustducin and transducin make the analogies of the rejection non-obvious. Regarding the carboxy terminus argument, the examiner had previously described the teachings of both Margolskee and Ruiz-Avila et al., which indicate that the carboxy terminus is important to the function of sensation-specific G proteins. Margolskee "the carboxy terminal 60 amino acids of all three proteins [gustducin and rod and cone transducins] are highly conserved, while the carboxyl terminal 38 amino acids are identical. The carboxyl terminal identity is of particular importance because it encompasses the site that has been implicated in G protein/receptor interactions" (col.9, lines 13-16). Yao et al. suggests "chimeric G_q variants and the isolated nucleic acids encoding the same. In one embodiment, the chimeric G_q protein variants comprise C-terminal sequences from transducin or $G\alpha_{olf}$." (col.3, lines 10-13) and Yao et al. teach that a preferred embodiment has "at least about five amino acids in the C terminus of the G_q-protein replace…up to 44 amino acids of the C terminus of transducin or $G\alpha_{olf}$ " (col.5, lines 16-19 and 22-23); the examiner believes there is ample suggestion of the claimed invention. Regarding the homology argument, the examiner had previously described the teachings of Margolskee who teaches "among mammals…the α subunits of gustducin and the transducins comprise a subfamily of closely related proteins" (col.8, lines 66-67 and col.9, lines 1-2). Ruiz-Avila et al. seems to suggest both (1) the strong homology between gustducin and the transducins and (2) the importance of the C-

terminus, "Several biochemical studies suggest that the interaction of gustducin with its cognate taste receptors is similar to that of transducin with rhodopsin. A key result of these studies is that the C terminus of α-gustducin is a critical determinant for its interaction with taste receptors" (page 8870, col.1, Results). So regarless of the overall "low 58% homology" between gustducin and transducin, the portion important for function (44 amino acids of the carboxy terminus), there is a much greater homology.

The applicant further argues (Remarks, page 10) that Ruiz-Avila et al. does not add to the teachings of Margolskee and Yao et al. to suggest the claimed chimeric G-protein. The applicant further suggests that Ruiz-Avila et al. would not have led a skilled artisan to expect success in making 'different' (only 58% homology) chimeric proteins based on the basic units taught by Ruiz-Avila. The examiner had previously reported that Yao et al. suggests "chimeric G_q variants and the isolated nucleic acids encoding the same. In one embodiment, the chimeric G_q protein variants comprise C-terminal sequences from transducin or $G\alpha_{olf}$." (col.3, lines 10-13) and Yao et al. teach that a preferred embodiment has "at least about five amino acids in the C terminus of the G_q-protein replace…up to 44 amino acids of the C terminus of transducin or $G\alpha_{olf}$ " (col.5, lines 16-19 and 22-23), while Ruiz-Avila et al., rather than indicating likelihood of lack of success, as suggested by the applicant, actually, indicates the transferability of information gathered from studying transducin to gustducin (page 8870, Results). It is the critical c-terminus which the instant claims seem to indicate is the point of novelty. Both Margolskee and Ruiz-Avila suggest that this portion of the gustducin molecule is critical for function. Neither the instant claims, nor the teachings of the cited art suggest

mutating the c-terminus; Therefore, the applicant's suggestion "58% homology" is slightly misleading. The examiner has not construed the teachings of the cited art to mean that there can only be a 58% homology of the C-terminus, neither is such limitation in the instant claims; the applicant has put forward this suggestion which is not at all what was described in the teachings of the cited art, regarding the critical c-terminus. The applicant takes Ruiz-Avila as indicating unpredictability, but the examiner interprets this art as reinforcing the criticality of the C-terminus. Together with the suggestion of Yao to make chimeric G-proteins comprising the c-terminus of transducin, the teachings of Margolskee and Ruiz-Avila indicate similarities between transducin and gustducin and collectively suggest $G_{\alpha q\text{-Gustducin}}$ chimeric G-protein comprising a substituted 44 amino acid carboxy terminus where such 44 amino acid unit of Gustducin is the last 44 amino acids of SEQ ID NO:2. There is really a low level of unpredictability, contrary to the applicant's assertion. The homologies suggested by the cited art confirm the predictability of the similar chimeric sense receptors.

The applicant attempts to traverse the combination of cited art by suggesting "the prior art does not disclose …any…chimera that is closely related to the claimed chimera" (Remarks, page 13, top parag.). Contrary to the applicant's assertion, the cited art, particularly Yao et al. teach a "chimeric G_q protein variants comprise C-terminal sequences from transducin…(col.3, lines 10-13)…[having]…up to 44 amino acids of the C terminus of transducin" (col.5, lines 16-19 and 22-23). The other cited art clearly suggest a strong homology between gustducin and transducin, thereby making

obvious an analogous chimeric G protein, having the 44 c-terminal amino acids from gustducin. These would be closely related chimera.

The applicant suggests that he is the first to invent, $G_{\alpha q\text{-}Gustducin}$ chimeric G-protein comprising a substituted 44 amino acid carboxy terminus where such 44 amino acid unit of Gustducin is the last 44 amino acids of SEQ ID NO:2 (Remarks, page 14). The applicant also asserts, "the references do not disclose or suggest the claimed protein." (Remarks, page 14). The examiner agrees that none of the cited references are 102-type references, exactly reciting the claimed invention. However, taken together they do suggest the claimed invention; the detailed rationale for combining the teachings have been discussed above, and are reiterated in the rejection below.

The applicant continues for a few more pages (remarks, pages 15-18), dissecting the various teachings of the cited art and reiterating previously presented arguments, variously emphasizing the "homology issue," the "inadequacy of the additional Ruiz-Avila reference to supplement the teachings of the 2 other cited references," and "lack of Yao to teach chimeric $G_{\alpha q\text{-}Gustducin}$." All of these arguments have been addressed.

Accordingly, the examiner finds the applicant's arguments unpersuasive and hereby maintains the instant rejection.

The examiner repeats the pending rejection below:

Claims 1-2, 6-13, and 18-34 are rejected under 35 U.S.C. 103(a) as being obvious over Margolskee (US-5,817,759, issued 6 October 1998) in view of Yao et al. (US-7,041,457, issued 9 May 2006) and further in view of Ruiz-Avila et al. (PNAS. July 17 2001. vol.98; No.15: 8868-8873).

Claim 1 is directed to a $G_{\alpha q\text{-}Gustducin}$ chimeric G-protein wherein the last 44 amino acids of the $G_{\alpha q}$ protein sequence are replaced with a 44 amino acid unit of Gustducin, where such 44 amino acid unit of Gustducin is the last 44 amino acids of SEQ ID NO:2.

Margolskee teaches "the α subunit of a novel taste receptor cell specific G protein, gustducin, or fragments and variants of the α subunit" (col. 3, lines 3-5). Margolskee teaches, "Gustducin α subunit variants…may comprise polypeptide analogs wherein one or more of the specified amino acids is deleted or replaced or wherein one or more nonspecified amino acids are added" (col.3, lines 48-51). Margolskee also teach "among mammals, a 1 to 3% difference in amino acids identity is typical among α isotypes, suggesting that the α subunits of gustducin and the transducins comprise a subfamily of closely related proteins" (col.8, lines 66-67 and col.9, lines 1-2). Margolskee "the carboxy terminal 60 amino acids of all three proteins [gustducin and rod and cone transducins] are highly conserved, while the carboxyl terminal 38 amino acids are identical. The carboxyl terminal identity is of particular importance because it encompasses the site that has been implicated in G protein/receptor interactions" (col.9, lines 13-16). In addition, Margolskee teach SEQ ID NO:3 which consists of the last 40 amino acids of Gustducin α subunit and is 100% identical to the last 40 of SEQ ID NO:2 of the instant application.

While Margolskee teach Gustducin α subunit variants and the importance of the carboxy 40 amino acids, Margolskee do not teach chimeric G-proteins comprising the carboxy 40 amino acids of Gustducin α subunit.

Yao et al. teach "chimeric G_q variants and the isolated nucleic acids encoding the same. In one embodiment, the chimeric G_q protein variants comprise C-terminal sequences from transducin or $G\alpha_{olf}$." (col.3, lines 10-13). Yao et al. teach that a preferred embodiment has "at least about five amino acids in the C terminus of the G_q-protein replace by at least about five amino acids from the C terminus of $G\alpha_{olf}$ or transducin" (col.5, line 16-19) and "up to 44 amino acids of the C terminus of transducin or $G\alpha_{olf}$ may be incorporated" (col.5, lines 22-23). Yao et al. indicated that the C-terminus of Gα proteins can be modified to promote promiscuity of taste receptors. Yao et al. also describe the shared homologies of Gα subunits. Further, Yao et al. also suggest that the gustducin-coupled bitter receptor can be modified to increase promiscuity with regard to GPCR coupling (col.4, lines 35-55). In particular, Yao et al. show that their chimeric G-protein wherein the C terminus of the G_q-protein is replaced by 44 amino acids of transducin has functional activity with the Taste Receptor (col.8, Table I, and Examples).

Ruiz-Avila et al. teach "Several biochemical studies suggest that the interaction of gustducin with its cognate taste receptors is similar to that of transducin with rhodopsin. A key result of these studies is that the C terminus of α-gustducin is a critical determinant for its interaction with taste receptors" (page 8870, col.1, Results).

Consequently, claim 1 would be obvious, in light of the teachings of Margolskee and Yao et al. and Ruiz-Avila et al.

Claim 2 is directed to the chimeric protein of claim 1, wherein the G-protein is a $G_{\alpha 15 \text{ or } 16\text{-Gustducin}}$. Margolskee teaches, $G_{\alpha 15}$ and $G_{\alpha 16}$ (col.2, line 4).

Claim 10 is directed to methods of producing a chimeric G-protein of claim 1 by recombinant technology. Margolskee teaches, "large scale production of gustducin α subunit polypeptides" by recombinant methods (col. 3, line 24-35). Margolskee teaches stably transformed host cells comprising the expression vector (col.3, line 24).

Claim 11 is directed to a method of analysis and discovery of modulators of bitter taste receptors using the chimeric proteins of claim 1. Margolskee teaches, "methods for identifying taste modifying agents having the capability to affect interactions between the gustducin α subunit and taste receptors or effectors and also describes methods for utilizing such taste modifying agents to modify taste by mimicking or inhibiting...bitter." (col. 4, lines 52-56).

Claims 12-13 directed to a method of claim 11, wherein the assay is a mammalian cell-based assay. Margolskee teaches such mammalian cell-based assays that measure changes in intracellular messengers, including phosphodiesterase (col.13, lines 4-21) which affects Ca^{2+} and IP3 production.

Claim 18 is directed to a $G_{\alpha q\text{-}Gustducin}$ chimeric G-protein wherein the last 44 amino acids of the $G_{\alpha q}$ protein sequence are replaced with a 44 amino acid unit of Gustducin, where such 44 amino acid unit of Gustducin is the last 44 amino acids of SEQ ID NO:2 and wherein the resulting $G_{\alpha q\text{-}Gust44}$ chimeric G-protein has a sequence homology of at least 80% in the last 44 amino acids of SEQ ID NO:2.

Margolskee teaches "the α subunit of a novel taste receptor cell specific G protein, gustducin, or fragments and variants of the α subunit" (col. 3, lines 3-5). Margolskee teaches, "Gustducin α subunit variants…may comprise polypeptide analogs

wherein one or more of the specified amino acids is deleted or replaced or wherein one or more nonspecified amino acids are added" (col.3, lines 48-51). Margolskee also teach "among mammals, a 1 to 3% difference in amino acids identity is typical among α isotypes, suggesting that the α subunits of gustducin and the transducins comprise a subfamily of closely related proteins" (col.8, lines 66-67 and col.9, lines 1-2). Margolskee "the carboxy terminal 60 amino acids of all three proteins [gustducin and rod and cone transducins] are highly conserved, while the carboxyl terminal 38 amino acids are identical. The carboxyl terminal identity is of particular importance because it encompasses the site that has been implicated in G protein/receptor interactions" (col.9, lines 13-16). In addition, Margolskee teach SEQ ID NO:3 which consists of the last 40 amino acids of Gustducin α subunit and is 100% identical to the last 40 amino acids of SEQ ID NO:2 of the instant application. Margolskee teaches, $G_{\alpha 15}$ and $G_{\alpha 16}$ (col.2, line 4). Margolskee teaches, "large scale production of gustducin α subunit polypeptides" by recombinant methods (col. 3, line 24-35). Margolskee teaches stably transformed host cells comprising the expression vector (col.3, line 24). Margolskee teaches, "methods for identifying taste modifying agents having the capability to affect interactions between the gustducin α subunit and taste receptors or effectors and also describes methods for utilizing such taste modifying agents to modify taste by mimicking or inhibiting...bitter." (col. 4, lines 52-56). Margolskee teaches such mammalian cell-based assays that measure changes in intracellular messengers, including phosphodiesterase (col.13, lines 4-21) which affects Ca^{2+} and IP3 production.

While Margolskee teach Gustducin α subunit variants and the importance of the carboxy 40 amino acids, Margolskee do not teach chimeric G-proteins comprising the carboxy 40 amino acids of Gustducin α subunit. Margolskee does not specifically teach the $G_{\alpha q\text{-Gustducin}}$ chimeric G-protein and also does not specifically recite replacement of the C-terminal sequence 44 amino acids of the gustducin receptor.

Yao et al. teach "chimeric G_q variants and the isolated nucleic acids encoding the same. In one embodiment, the chimeric G_q protein variants comprise C-terminal sequences from transducin or $G\alpha_{olf}$." (col.3, lines 10-13). Yao et al. teach that a preferred embodiment has "at least about five amino acids in the C terminus of the G_q-protein replace by at least about five amino acids from the C terminus of $G\alpha_{olf}$ or transducin" (col.5, line 16-19) and "up to 44 amino acids of the C terminus of transducin or $G\alpha_{olf}$ may be incorporated" (col.5, lines 22-23). Yao et al. indicated that the C-terminus of Gα proteins can be modified to promote promiscuity of taste receptors. Yao et al. also describe the shared homologies of Gα subunits. Further, Yao et al. also suggest that the gustducin-coupled bitter receptor can be modified to increase promiscuity with regard to GPCR coupling (col.4, lines 35-55). In particular, Yao et al. show that their chimeric G-protein wherein the C terminus of the G_q-protein is replaced by 44 amino acids of transducin has functional activity with the Taste Receptor (col.8, Table I, and Examples).

Yao et al. teach, $G_{\alpha q}$ chimeric G-proteins (col.4, lines 12-27). In particular, the chimeric proteins described, combine various $G\alpha_q$ class proteins. Yao et al. also teach

chimeric G-proteins that comprise C-terminal sequences from Transducin and $G\alpha_{olf}$ (col3, lines 12-13).

Yao et al. also teach analysis and discovery of agonists and antagonists of chemosensory receptors, using G_q-protein variants (col.3, lines 15-30), including the "gustducin-coupled bitter receptor" (col.4, line 53). Yao et al. further suggest that modulators could be used in "protein pharmaceutical and food industries" (col.4, line 32). Yao et al. teach that a preferred embodiment has "at least about five amino acids in the C terminus of the G_q-protein replace by at least about five amino acids from the C terminus of $G\alpha_{olf}$ or transducin" (col.5, line 16-19) and "up to 44 amino acids of the C terminus of transducin or $G\alpha_{olf}$ may be incorporated" (col.5, lines 22-23). Consequently, claims 3-4 would be obvious, in light of the teachings of Yao et al.

While Yao et al. also teach chimeric G-proteins that comprise C-terminal sequences from Transducin and $G\alpha_{olf}$ (col3, lines 12-13) and Yao et al. indicated that the C-terminus of Gα proteins can be modified to promote promiscuity of taste receptors, Yao et al. does not specifically teach a $G\alpha_{q\text{-}Gustducin}$ chimeric G-protein having a C-terminal 44 amino acid substitution from Gustducin.

Ruiz-Avila et al. teach the nexus of gustducin and transducin homology and the importance of the C-terminus for interacting with taste receptors. Ruiz-Avila et al. teach "Several biochemical studies suggest that the interaction of gustducin with its cognate taste receptors is similar to that of transducin with rhodopsin. A key result of these studies is that the C terminus of α-gustducin is a critical determinant for its interaction with taste receptors" (page 8870, col.1, Results).

Consequently, all of the instant claims would be obvious, in light of the teachings of Margolskee and Yao et al. and Ruiz-Avila et al.

It would have been obvious to the person of ordinary skill in the art at the time of the invention was made to make a $G_{\alpha q}$ protein sequence are replaced with a 44 amino acid unit of Gustducin, where such 44 amino acid unit of Gustducin is the last 44 amino acids of Gustducin.

The person of ordinary skill in the art would have been motivated to make this protein because, "C-terminal substitution increases promiscuity of said variant G, protein as compared to the corresponding native G_q protein" (Yao et al. col.5, lines 20-22). While Yao et al. does not specifically teach making a chimera between G_q protein and gustducin, it is clearly obvious in light of the teachings involving substitutions with C-terminal sequences from other chemosensory molecules, transducin and $G\alpha_{olf}$). In particular, Yao et al. show that their chimeric G-protein wherein the C terminus of the G_q-protein is replaced by 44 amino acids of transducin has functional activity with the Taste Receptor (col.8, Table I, and Examples). Additionally, Margolskee teach that the carboxy terminal 40 amino acids of Gustducin are important for G protein/receptor interactions. Furthermore, Margolskee teach "the carboxy terminal 60 amino acids of all three proteins [gustducin and rod and cone transducins] are highly conserved, while the carboxyl terminal 38 amino acids are identical." Ruiz-Avila et al. teach "Several biochemical studies suggest that the interaction of gustducin with its cognate taste receptors is similar to that of transducin with rhodopsin. A key result of these studies is that the C terminus of α-gustducin is a critical determinant for its interaction with taste

receptors" (page 8870, col.1, Results). Furthermore, Yao et al. suggest that analysis and discovery of agonists and antagonists of chemosensory receptors, using G_q-protein variants can be performed using chimeric proteins and actually mention gustducin bitter receptor as a receptor which might be useful "to customize sensory perception" (col.4, line 32-33).

In addition, to the strong suggestion to make a $G_{\alpha q}$ protein sequence are replaced with a 44 amino acid unit of Gustducin, where such 44 amino acid unit of Gustducin is the last 44 amino acids of Gustducin by the combined teachings of Margolskee in view of Yao et al. and further in view of Ruiz-Avila et al., there is another rationale for combining prior art elements according to known methods to yield predictable results. All of the claimed elements were known in the prior art and one skilled in the art could have combined the element as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Each of the elements (chimeric $G\alpha_q$-proteins and methods of using them; a suggestion of the importance of the c-terminal 44 amino acids of Gustducin and related G-proteins; knowledge that the C terminus of α-gustducin is a critical determinant for its interaction with taste receptors; and the knowledge that the C-terminus of Gα proteins can be modified to promote promiscuity of taste receptors) are taught by Margolskee or Yao or Ruiz-Avila et al. It would be therefore predictably obvious to use a combination of these elements in a vaccine. The methods of using these chimeric G-proteins are further known in the art and are predictable; therefore they are likewise obvious.

An artisan would have expected success, because Yao et al. were successful in making similar chimeric G-proteins with other chemosensory receptors. Absent evidence to the contrary, there is no reason to believe that making a $G_{\alpha q}$ protein sequence are replaced with a 44 amino acid unit of Gustducin, where such 44 amino acid unit of Gustducin is the last 44 amino acids of Gustducin would not be successful.

Therefore the products and methods as taught by Margolskee in view of Yao et al. and further in view of Ruiz-Avila et al. would have been *prima facie* obvious over the method of the instant application.

Conclusion

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claims are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**. The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SDL/ Scott Long
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